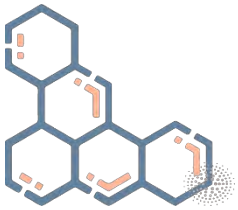
# Methylmalonic Aciduria

# Precision Panel



## Overview

Methylmalonic Aciduria/Acidemia (MMA) is an autosomal recessive disorder of the amino acid metabolism with a defect localized in the conversion of methylmalonyl-coenzyme A (CoA) into succinyl-CoA. The body is therefore unable to process certain proteins and lipids properly. This causes an accumulation of methylmalonic acid in the organisms which manifests in the form of neurologic symptoms such as seizures, encephalopathy, and stroke. It is a lethal, severe heterogeneous disorder involving methylmalonate and cobalamin metabolism with poor prognosis. This disorder can be identified isolated or combined with other organic acidemias.

The Igenomix Methylmalonic Aciduria Precision Panel can be used to make an accurate and directed diagnosis ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

## Indications

The Igenomix Methylmalonic Aciduria/Acidemia Precision Panel is indicated for those patients with a clinical suspicion or diagnosis with or without the following manifestations:

- Vomiting
- Dehydration
- Lethargy
- Seizures
- Recurrent infections
- Progressive encephalopathy
- Hypotonia
- Developmental delay
- Hepatomegaly
- Intellectual disability

## Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient.

- Early initiation of treatment with a multidisciplinary team in the form of nutritional dietary modifications, prevention and treatment of infections.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

## Genes & Diseases

| GENE | OMIM DISEASES | INHERITANCE* | % GENE COVERAGE (20X) | HGMD** |
|---|---|---|---|---|
| *ABCD4* | Methylmalonic Aciduria And Homocystinuria | AR | 100 | 8 of 8 |
| *ACSF3* | Combined Malonic And Methylmalonic Aciduria | AR | 100 | 27 of 27 |
| *CCN6* | Progressive Pseudorheumatoid Arthropathy Of Childhood | AR | 100 | NA of NA |
| *CD320* | Methylmalonic Aciduria | AR | 89 | 2 of 2 |
| *HCFC1* | Methylmalonic Acidemia And Homocysteinemia, X-linked Non-Syndromic Intellectual Disability | X,XR,G | 99.81 | NA of NA |
| *LMBRD1* | Methylmalonic Aciduria And Homocystinuria | AR | 99.88 | 8 of 8 |
| *MCEE* | Methylmalonyl-CoA Epimerase Deficiency | AR | 100 | 5 of 6 |
| *MLYCD* | Malonyl-CoA Decarboxylase Deficiency | AR | 93.84 | 32 of 40 |
| *MMAA* | Methylmalonic Aciduria | AR | 99.98 | 77 of 77 |
| *MMAB* | Methylmalonic Aciduria | AR | 99.52 | 43 of 43 |
| *MMACHC* | Methylmalonic Aciduria And Homocystinuria | AR | 99.97 | 105 of 105 |
| *MMADHC* | Methylmalonic Aciduria And Homocystinuria | AR | 99.63 | 20 of 20 |
| *MMUT* | Methylmalonic Aciduria Due To Methylmalonyl-CoA Mutase Deficiency | AR | 99.97 | NA of NA |
| *MTR* | Methylcobalamin Deficiency, Folate-Sensitive Neural Tube Defects | AR | 99.94 | 42 of 45 |
| *PRDX1* | Methylmalonic Aciduria And Homocystinuria | AR | 100 | 3 of 3 |
| *SUCLA2* | Mitochondrial DNA Depletion Syndrome (Encephalomyopathic With Or Without Methylmalonic Aciduria) | AR | 100 | 27 of 27 |
| *SUCLG1* | Mitochondrial DNA Depletion Syndrome (Encephalomyopathic Type With Methylmalonic Aciduria) | AR | 100 | 34 of 34 |
| *TCN2* | Transcobalamin Deficiency | AR | 100 | 25 of 27 |

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

## Methodology


## Contact us

**Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:**

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

# References

1. Sloan, J. L., Johnston, J. J., Manoli, I., Chandler, R. J., Krause, C., Carrillo-Carrasco, N., Chandrasekaran, S. D., Sysol, J. R., O'Brien, K., Hauser, N. S., Sapp, J. C., Dorward, H. M., Huizing, M., NIH Intramural Sequencing Center Group, Barshop, B. A., Berry, S. A., James, P. M., Champaigne, N. L., de Lonlay, P., Valayannopoulos, V., … Venditti, C. P. (2011). Exome sequencing identifies ACSF3 as a cause of combined malonic and methylmalonic aciduria. *Nature genetics*, *43*(9), 883–886. https://doi.org/10.1038/ng.908
2. Matsui, S. M., Mahoney, M. J., & Rosenberg, L. E. (1983). The natural history of the inherited methylmalonic acidemias. *New England Journal of Medicine, 308*(15), 857-861. doi:10.1056/nejm198304143081501
3. Zhou, X., Cui, Y., & Han, J. (2018). Methylmalonic acidemia: Current status and research priorities. *Intractable & rare diseases research*, *7*(2), 73–78. https://doi.org/10.5582/irdr.2018.01026
4. Deodato, F., Boenzi, S., Santorelli, F. M., & Dionisi-Vici, C. (2006). Methylmalonic and Propionic Aciduria. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics, 142C*(2), 104-112. doi:10.1002/ajmg.c.30090
5. Miousse, I. R., Watkins, D., Coelho, D., Rupar, T., Crombez, E. A., Vilain, E., . . . Rosenblatt, D. S. (2009). Clinical and molecular heterogeneity in patients with the cbld inborn error of cobalamin metabolism. *The Journal of Pediatrics, 154*(4), 551-556. doi:10.1016/j.jpeds.2008.10.043
6. Carrillo-Carrasco, N., Chandler, R. J., & Venditti, C. P. (2011). Combined methylmalonic acidemia And homocystinuria, cblC type. I. Clinical Presentations, diagnosis and management. *Journal of Inherited Metabolic Disease, 35*(1), 91-102. doi:10.1007/s10545-011-9364-y